# Visualization of Breast Microcalcifications on Digital Breast Tomosynthesis and 2-Dimensional Digital Mammography Using Specimens

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**ABSTRACT**

**PURPOSE:** The purpose of this study is to compare the visibility of microcalcifications of digital breast tomosynthesis (DBT) and full-field digital mammography (FFDM) using breast specimens.
**MATERIALS AND METHODS:** Thirty-one specimens' DBT and FFDM were retrospectively reviewed by four readers.
**RESULTS:** The image quality of microcalcifications of DBT was rated as superior or equivalent in 71.0% by reader 1, 67.8% by reader 2, 64.5% by reader 3, and 80.6% by reader 4. The Fleiss kappa statistic for agreement among readers was 0.31.
**CONCLUSIONS:** We suggest that image quality of DBT appears to be comparable with or better than FFDM in terms of revealing microcalcifications.

**KEYWORDS:** Breast microcalcification, digital breast tomosynthesis, full-field digital mammography

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## Introduction

Since 1990, the death rate from breast cancer has decreased by nearly 34% in the United States. Mammography screening has been important in this shift. Screening mammography for breast cancer has led to earlier detection and more timely and effective treatment.[1] However, the overlap of tissues depicted on mammography may create significant obstacles to the detection and diagnosis of abnormalities.[2]

Breast density is now recognized as one of the strongest risk factors for breast malignancy. Several studies were conducted to examine differences in breast density assessed on different image types. Tagliafico et al showed that breast density values in digital breast tomosynthesis (DBT) were lower than those obtained using 2-dimensional full-field digital mammography (FFDM) according to the Breast Imaging Reporting and Data System (BI-RADS).[3–5] When small microcalcifications (<1 mm) are overlapped with breast tissues, they become difficult to detect and have limitation to visualization on mammography.[6] Superimposition of overlapping breast density can also obscure microcalcifications.

Digital breast tomosynthesis is a relatively new modality that is a tomographic application of digital mammography. Digital breast tomosynthesis allows for reconstructing planes from breast tissue volume viewed in sequential sections through the breast and potentially overcomes the inherent limitations of mammography caused by the overlapping normal and pathological tissues during standard 2-dimensional projections. Digital breast tomosynthesis offers potential advantages for evaluating masses, areas of architectural distortion, and asymmetries that exceed those of conventional mammographic images. A number of studies have compared the clinical performance using DBT and FFDM in terms of masses, architectural distortions, and asymmetries and have concluded that DBT shows superior image quality compared with FFDM in characterizing masses and asymmetry. Studies also reported that DBT could be even more efficient by reducing recall rates and additional image studies.[7–18] And, several studies demonstrated that combination of DBT with FFDM was superior for cancer detection.[19–21]

In addition to masses, architectural distortions, and asymmetries, microcalcifications are one of the most commonly appearing abnormalities in screening mammography. In a significant proportion of breast cancer cases, detecting microcalcifications on mammography is an important task for identifying the presence of breast lesions, especially in cases of nonpalpable lesions. In addition, microcalcifications are often the sole mammographic features that indicate the presence of a tumor.[22,23] Approximately 40% of mammary carcinoma presents such microcalcification.[23] In addition, up to 90% of ductal carcinoma in situ (DCIS) are found in their preclinical, asymptomatic phase by detecting microcalcifications on mammography.[24]

The current strategy for evaluating and managing microcalcifications makes the important assumption that the microcalcifications are present within or are closely related to the most

important underlying pathologic change in the breast. Thus, specimen mammography was undergone after diagnostic biopsy and surgical excision for breast lesion with microcalcifications to determine whether the targeted microcalcifications had been included adequately.[25,26]

To date, very few studies in the literature have compared the visibility of microcalcifications in FFDM and DBT.[27] Spangler et al[9] reported that overall sensitivity of FFDM was higher than for DBT (84% and 75%, respectively). These results are similar to the comparative study by Poplack et al.[11] Their study determined that calcifications accounted for 73% (8/11) of the cases in which tomosynthesis had inferior image quality. However, Kopans et al[28] compared the clarity with which microcalcifications were seen on mammography with DBT. Their results showed that in 41.6% of the cases, microcalcifications were seen with superior clarity with DBT; 50.4% of the cases visibility was the same for both DBT and mammography and 8% of cases microcalcifications were seen with greater clarity on mammography. Also, Destounis et al[29] assessed the image quality of DBT as equivalent or superior in 92.2% of cases. Thus, there has been no definitive consensus in the recent literature regarding characterizing and detecting microcalcifications with DBT. In this study, we compared the visualization and image quality of microcalcifications imaged with DBT and FFDM using breast specimens.

## Materials and Methods

### *Case and data collections*

This study was approved by our institutional review board, and written informed consent was waived.

From December 2013 to April 2014, 31 excision specimens in 30 patients' (age range: 30-66 years; mean age: 49.6 years) radiographies were included in this retrospective study.

Among 31 specimens, 25 cases were performed core needle biopsy prior to the surgical excision. Of the 25 biopsied cases, 10 cases showed malignant results, and 15 cases were benign. Surgical excisions for biopsy confirmed benign lesions were performed due to patients' demand, and patients with "high risk factors." The remaining 6 nonbiopsied cases were also undergone surgical excision due to same reasons.

Excisional specimen mammography was performed with FFDM followed by DBT by a trained, dedicated technologist using a commercially available device (Selenia Dimensions system; Hologic, Inc., Bedford, MA, USA). The device consisted of a custom-designed high-power (mA) tungsten (W) anode x-ray tube and rhodium, silver, and aluminum x-ray filters. Different filters in DBT and FFDM imaging modes produce optimal x-ray spectra (20-49 kVp) based on the thickness and composition of the breast using automatic exposure control. The image receptor was a 70-μm pixel pitch selenium direct capture detector. The x-ray tube moved over a 15° arc.

### *Image analysis*

Preoperative mammographic breast composition was evaluated subjectively, according to the BI-RADS category. Five cases (16.1%) were classified as scattered areas of fibroglandular density, 19 (61.3%) as heterogeneous dense, and 7 (22.6%) as extremely dense.[30] In addition, BI-RADS category was assigned to microcalcifications (Table 1).

Four radiologists with 2 to 11 years of experience practicing radiology and with 2 months (readers 3 and 4) to 4 years (readers 1 and 2) of experience in DBT interpretation participated in this study. All readers were blinded to the pathologic results. The 2 modalities were compared at workstations (SecurView, Hologic, Inc.) that could slice images to any thickness up to the specimen thickness and magnify the specific area. Adjusting of window level and window width was permitted. The reviewers were given unlimited time to page back and forth through the DBT images and to review the mammography.

The radiologist subjectively rated the visibility of microcalcifications, by stating that the FFDM was better, DBT was better, or both FFDM and DBT were equivalent. Visibility of microcalcifications was defined as sharper visualization with better contrast against the background of the breast parenchyma.

Visibilities of the microcalcifications according to the different slab thicknesses on DBT were also evaluated. We changed the thicknesses to 1, 5, and 10 mm.

### *Statistical analysis*

Exact 95% confidence intervals (CIs) based on binomial distribution were calculated for each of the cases that had been judged to be seen more clearly on DBT. The Fleiss kappa for inter-reader agreement was also calculated. We used the following definitions to interpret the kappa coefficient: less/equal to 0 indicates poor agreement, 0.01 to 0.20 slight agreement, 0.21 to 0.40 fair agreement, 0.41 to 0.60 moderate agreement, 0.61 to 0.80 substantial agreement, 0.81 to 0.99 almost perfect agreement, and 1.00 perfect agreements.[20,31] Either a $\chi^2$ or the Fisher exact test was used to compare malignant and benign lesions.

*P* values of less than .05 were considered statically significant, and the statistical analyses were performed using STATA 12.0 (Stata Corporation, College Station, TX, USA) and SPSS 21.0 (SPSS, Chicago, IL, USA).

## Results

### *Characteristics of the specimens*

For preoperative analysis by BI-RADS categories, among the 31 cases, 1 (3.2%) was classified as BI-RADS category 3 microcalcifications, 26 (83.9%) were 4, 2 (6.4%) were 5, and 2 (6.4%) were 6 (Table 1). Distributions of microcalcifications were regional in 3 specimens (9.7%), grouped in 16 specimens (51.6%), and segmental in 12 specimens (38.7%). Microcalcifications were classified as coarse heterogeneous

**Table 1.** BI-RADS classifications for breast composition and microcalcifications.

| | NO. (%) |
|---|---|
| **Composition** | |
| Almost entirely fatty | 0 (0.0) |
| Scattered areas of fibroglandular density | 5 (16.1) |
| Heterogeneously dense | 19 (61.3) |
| Extremely dense | 7 (22.6) |
| **BI-RADS category** | |
| 3 | 1 (3.2) |
| 4A | 18 (58.1) |
| 4B | 6 (19.4) |
| 4C | 2 (6.4) |
| 5 | 2 (6.4) |
| 6 | 2 (6.4) |

Abbreviation: BI-RADS, Breast Imaging Reporting and Data System.

**Table 2.** Pathology results.

| PATHOLOGY RESULT | NO. (%) |
|---|---|
| **Benign (n = 20)** | |
| Fibrocystic change | 12 (60) |
| Usual ductal hyperplasia | 1 (5) |
| Florid ductal hyperplasia | 1 (5) |
| Sclerosing adenosis | 1 (5) |
| Columnar cell change | 1 (5) |
| Benign | 4 (20) |
| **Malignant (n = 11)** | |
| DCIS | 6 (54.5) |
| IDC | 4 (36.4) |
| DCIS with IDC | 1 (9.1) |

Abbreviations: DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma.

shape in 4 (12.9%), amorphous shape in 13 (41.9%), fine pleomorphic shape in 13 (41.9%), and fine linear shape in 1 (3.2%).

Specimen thickness ranged from 18 to 27 mm (mean thickness: 21.2 mm). Of the 31 specimens, 21 (64.5%) were benign and 11 (35.5%) were malignant. The malignant lesions were DCIS (n = 6, 54.5%), invasive ductal carcinoma (n = 4, 36.4%), and coexistence of both (n = 1, 9.1%). The benign lesions included fibrocystic changes (n = 12, 60%), usual ductal hyperplasia (n = 1, 5%), florid ductal hyperplasia (n = 1, 5%), sclerosing adenosis (n = 1, 5%), columnar cell change (n = 1, 5%), and unspecified benign (Table 2).

### *Microcalcifications visibility on DBT and FFDM*

Reader 1 perceived that the visibility of microcalcifications on DBT was superior in 15 of the 31 specimens (48.4%, 95% CI: 30.15%-66.94%) and equal to in 7 of 31 specimens (22.6%, 95% CI: 9.59%-41.40%). Reader 2 chose that the DBT images were superior in 18 of 31 specimens (58.1%, 95% CI: 38.08%-75.45%) and equal to in 3 specimens (9.7%, 95% CI: 2.04%-25.75%). Reader 3 perceived that the DBT images were superior in 15 of 31 specimens (48.4%, 95% CI: 30.15%-66.94%) and equal to in 5 specimens (16.1%, 95% CI: 5.45%-33.73%). Reader 4 preferred that the DBT images were superior in 25 of 31 specimens (80.7%, 95% CI: 62.53%-92.55%) and no cases in equal to (0%, 95% CI: 0%-11.22%). All readers preferred the DBT microcalcification images to those from FFDM. There is no difference in preference by difference in experience of DBT interpretation. The Fleiss kappa statistic for agreement among 4 readers was 0.31 (Table 3).

By slab thickness, all readers graded as better or equal at 1 mm than 5 mm and ranges varied from 93.6% to 100%. Reader 1 graded 22 DBT cases (71.0%, 95% CI: 51.96%-85.78%) as better at 1 mm than 5 mm and 8 cases (25.8%, 95% CI: 11.86%-44.61%) as equal in 1 and 5 mm. Reader 2 graded 10 DBT cases (32.3%, 95% CI: 16.68%-51.37%) as better at 1 mm than 5 mm and 20 cases (64.5%, 95% CI: 45.37%-80.77%) as equal in 1 and 5 mm. Reader 3, meanwhile, graded 26 DBT cases (83.9%-95% CI: 66.27%-94.55%) as better at 1 mm but perceived no cases as superior at 5 mm. Reader 4, graded 20 DBT cases (64.5%, 95% CI: 45.37%-80.77%) as better at 1 mm and 9 cases (29.1%, 95% CI: 14.22%-48.04%) as equal in 1 and 5 mm. All readers except for reader 2 graded better imaging qualities in 1 mm slap thickness, and all readers considered 1 mm as better than or equal to 5 mm (Table 4).

In comparing 1 mm versus 10 mm slice thickness and 5 mm versus 10 mm slice thickness, all readers preferred thin slice thickness also. Reader 3 did not prefer 10 mm thickness in any cases (Table 4).

There were a total of 11 histologically proven malignancies and 20 benign findings. The readers 1 and 2 chose DBT as having a superior or equivalent image quality for malignancies in 10 (90.9%, $P = .1$). Readers 3 and 4 rated DBT as superior or equivalent image quality for malignancies in 8 (72.7%, $P = 0.7$). For benign lesions, the preference for DBT was slightly higher in reader 4. But these differences were not significant (Table 5, Figures 1 and 2).

## Discussion

Previous clinical experience with DBT for assessing breast microcalcifications had revealed possible pitfalls, and few studies had compared DBT and FFDM for evaluating microcalcifications.[9,11,27–29]

Our study focused on evaluating visualization of microcalcifications in specimens on DBT and FFDM. As the data

**Table 3.** Readers' preferences between DBT and FFDM.

| | DBT > FFDM (%) | DBT = FFDM (%) | DBT < FFDM (%) | 95% CI[A] |
|---|---|---|---|---|
| Reader 1 | 15 (48.4) | 7 (22.6) | 9 (29.0) | 52.96–85.78 |
| Reader 2 | 18 (58.1) | 3 (9.7) | 10 (32.2) | 45.37–80.77 |
| Reader 3 | 15 (48.4) | 5 (16.1) | 11 (35.5) | 45.37–80.77 |
| Reader 4 | 25 (80.7%) | 0 (0) | 6 (19.3) | 62.53–92.55 |

Abbreviations: CI, confidence interval; DBT, digital breast tomosynthesis; FFDM, full-field digital mammography.
[A]95% CI for DBT>FFDM and DBT=FFDM.

**Table 4.** Readers' preferred DBT thicknesses (%).

| | 1 MM > 5 MM (%) | 1 MM = 5 MM (%) | 1 MM < 5 MM (%) | 95% CI[A] |
|---|---|---|---|---|
| Reader 1 | 22 (71.0) | 8 (25.8) | 1 (3.2) | 83.30–99.92 |
| Reader 2 | 10 (32.3) | 20 (64.5) | 1 (3.2) | 83.30–99.92 |
| Reader 3 | 26 (83.9) | 5 (16.1) | 0 (0) | 88.78–1 |
| Reader 4 | 20 (64.5) | 9 (29.1) | 2 (6.4) | 78.58–99.21 |
| | 1 MM > 10 MM (%) | 1 MM = 10 MM (%) | 1 MM < 10 MM (%) | 95% CI[B] |
| Reader 1 | 25 (80.7) | 5 (16.1) | 1 (3.2) | 83.30–99.92 |
| Reader 2 | 17 (54.8) | 13 (42.0) | 1 (3.2) | 83.30–99.92 |
| Reader 3 | 27 (87.1) | 4 (12.9) | 0 (0) | 88.78–100 |
| Reader 4 | 20 (64.5) | 8 (25.8) | 3 (9.7) | 74.25–97.96 |
| | 5 MM > 10 MM (%) | 5 MM = 10 MM (%) | 5 MM < 10 MM (%) | 95% CI[C] |
| Reader 1 | 9 (29.0) | 22 (71.0) | 0 (0) | 88.78–100 |
| Reader 2 | 15 (48.4) | 16 (51.6) | 0 (0) | 88.78–100 |
| Reader 3 | 17 (54.8) | 14 (45.2) | 0 (0) | 88.78–100 |
| Reader 4 | 11 (35.5) | 17 (54.8) | 3 (9.7) | 74.25–97.96 |

Abbreviations: CI, confidence interval; DBT, digital breast tomosynthesis; FFDM, full-field digital mammography. 95% CI for DBT > FFDM and DBT = FFDM.
[a]95% CI for 1 mm > 5 mm and 1 mm = 5 mm.
[b]95% CI for 1 mm > 10 mm and 1 mm = 10 mm.
[c]95% CI for 5 mm > 10 mm and 5 mm = 10 mm.

**Table 5.** Numbers of superiorly or equally visible cases on DBT and FFDM according to the pathology results (%).

| | READER 1 | | READER 2 | |
|---|---|---|---|---|
| | MALIGNANCY (n = 11) | BENIGN (n = 20) | MALIGNANCY (n = 11) | BENIGN (n = 20) |
| DBT ⩾ FFDM | 10 (90.9%) | 12 (60.0%) | 10 (90.9%) | 11 (55.0%) |
| DBT < FFDM | 1 (9.1%) | 8 (40.0%) | 1 (9.1%) | 9 (45.0%) |
| *P* value | .1 | | .055 | |
| | READER 3 | | READER 4 | |
| | MALIGNANCY (n = 11) | BENIGN (n = 20) | MALIGNANCY (n = 11) | BENIGN (n = 20) |
| DBT ⩾ FFDM | 8 (72.7%) | 12 (60.0%) | 8 (72.7%) | 17 (85.0%) |
| DBT < FFDM | 3 (27.3%) | 8 (40.0%) | 3 (27.3%) | 3 (15.0%) |
| *P* value | .7 | | .6 | |

Abbreviations: DBT, digital breast tomosynthesis; FFDM, full-field digital mammography.

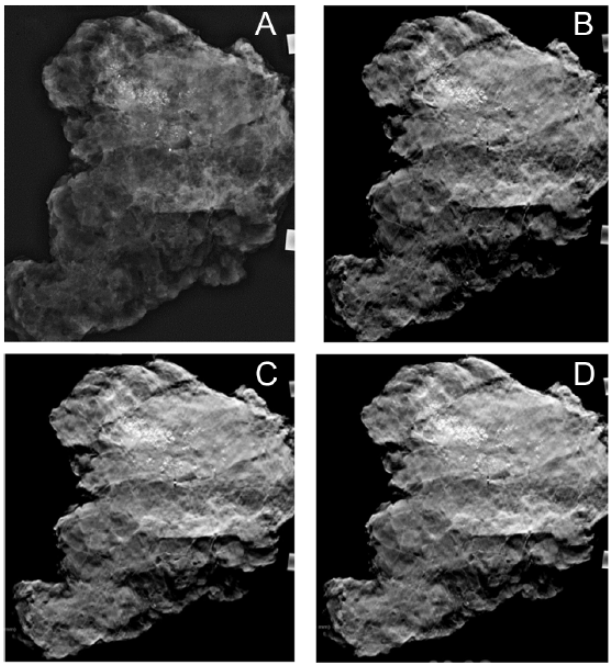


**Figure 1.** Specimen with invasive ductal carcinoma on (A) FFDM and (B) DBT. Reconstructed 1 mm slice of specimen (B) DBT shows clearer microcalcifications than (A) FFDM. The 1 mm slice (B) DBT shows clearer microcalcifications compared with (C) 5 mm DBT or (D) 10 mm DBT. DBT indicates digital breast tomosynthesis; FFDM, full-field digital mammography.

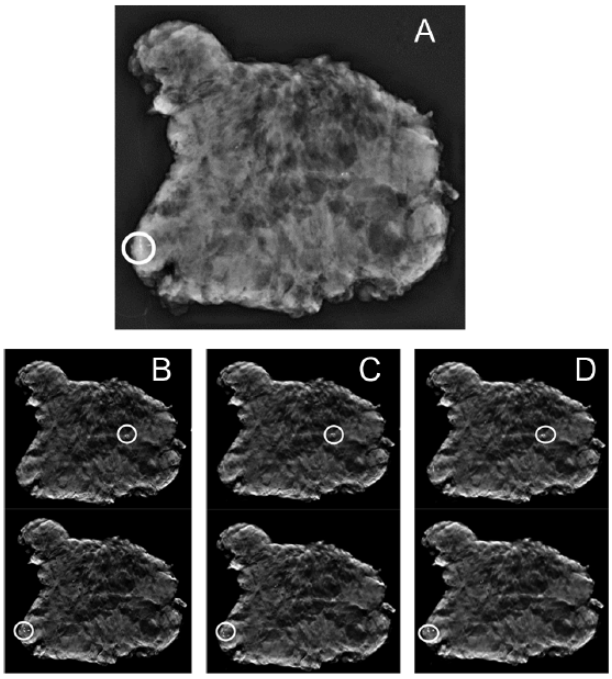


**Figure 2.** Specimen with benign lesions on (A) FFDM and (B) DBT. Two grouped microcalcifications are more clearly demonstrated in reconstructed 1 mm slice of specimen (B) DBT than (A) FFDM. The (B) 1 mm slice DBT shows clearer microcalcifications compared with (C) 5 mm DBT or (D) 10 mm DBT. DBT, digital breast tomosynthesis; FFDM, full-field digital mammography.

showed, all readers tended to prefer DBT for microcalcification visibility, supporting an early report by Kopans et al.[28] The microcalcifications that were partially obscured by normal breast tissue were not seen well on FFDM, but DBT generates multiple projections by rotating the x-ray arm over a limited angular range; consequently, by reducing the structure noise of the normal breast, microcalcifications that were hidden on FFDM were more clearly seen on DBT.[32,33] A recent publication by Peters et al[34] compared FFDM, DBT, and synthetically reconstructed 2-dimensional images obtained from phantom and also found that DBT showed superior in visualization of microcalcifications than FFDM.

Some previous studies showed DBT was inferior modality to the FFDM for demonstrating microcalcifications. They suggested the lengthy exposure time of the tomosynthesis acquisition may have introduced motion-related blur, obscuring additional microcalcifications, and morphology of microcalcifications.[11] As our study was designed to use specimen, motions related blurring did not affect image quality. In this point, with technologic modifications for reducing acquisition time, image quality of microcalcifications on DBT could be much better than that on FFDM.

All, readers perceived much greater visualization of microcalcifications at 1 mm DBT slab thickness than at 5 or 10 mm thickness. Previous study by Poplack suggested that a 1 mm slice thickness might be too thin to show the clustered distribution of calcifications and small, clustered microcalcifications might be unobserved because that were not contained in a single slice.[11] In contrast, our study results showed that 1 mm slice thickness could contain these small clusters.

A detection study by Splanger et al[9] determined that FFDM was slightly more sensitive than tomosynthesis for the detection of microcalcifications. They adduced that the factor of the lower sensitivity of DBT was thin slice thickness. Although increasing the slice thickness will increase the ability to perceive a distribution of microcalcifications in the breast, the spatial resolution of each individual calcification is compromised with slabbing. Slab thickness can be tailored by clinical radiologist during assessing the DBT images. Radiologists could optimize slab thickness for specific purpose such as detection or characterization of microcalcifications. Thus, we suggest that by applying this function, the DBT could be better than the FFDM for evaluating the microcalcifications.

In this study, all readers agreed that DBT was superior or equivalent to FFDM in terms of visualizing microcalcifications. Our results are discordant with recent study by Clauser et al[35]; they concluded that there were no significant differences between wide scan-angle DBT and FFDM for detection and characterization of microcalcifications. This could be related to different scan settings and small sample sizes. We performed FFDM and DBT for excision specimens, and specimen mammography might be different from routine screening mammography. We found slight inter-reader agreement

(*K*: 0.31). This result is comparable with recent study which showed significant inter-reader differences about visibility of microcalcifications.[35] Readers with little experience with DBT also preferred DBT for evaluation of microcalcifications. This result is similar to those of a prior study by Smith et al[36] that showed that DBT could improve diagnostic performance and reduce recall rates even in less experienced radiologists. Thus, some degree of training is necessary for detecting and identifying microcalcifications on DBT.

All readers perceived the DBT demonstrated microcalcifications in malignant lesions better or at least equally than FFDM in malignant lesions, although the results were not statistically significant under the study conditions. For benign lesions, visibility of microcalcifications was slightly lower on DBT. This result is in agreement with recent study by Clauser et al[35] showed lower visibilities for benign lesions. They concluded that this could be related to lesion distribution or different natures of microcalcifications and associated findings.

Specimen radiography is a long established procedure for confirming the presence of both calcified and noncalcified targeted lesions after core needle biopsy and surgical excision.[25,26] After FFDM was approved by the US Food and Drug Administration in 2000, digital mammography has been used as specimen radiography but with significant loss of sensitivity compared with screen or film mammography.[37] The result that conspicuity of microcalcifications in DBT is better than or equal to FFDM suggests that DBT could compensate the defect of FFDM in the field of specimen radiography.

Our study had a number of limitations. First, the study included only 31 specimens, resulting in relatively large 95% CI and low statistical significance. Second, this study was designed to compare DBT with FFDM for microcalcification visualization but not detection. Moreover, we did not classify the microcalcifications by BI-RADS category, but characteristics such as size, distribution, form, and density could be clues to potential malignancy.[30,38] A previous study that focused on characterizing mass lesions showed that DBT improved the efficiency of diagnosing breast lesions by reducing the associated costs of additional imaging studies and unnecessary biopsies.[15] In the same manner, a study that compared 2 modalities for characterizing microcalcifications is necessary.

Finally, each obtained specimen was placed in a conventional specimen container for the DBT, and these containers produce artifacts in DBT reconstructions. Furthermore, in DBT, the regularly spaced grids impose additional artifacts within each specimen's imaging planes, causing image degradation.[39] Future efforts are needed to reduce these reconstruction artifacts in DBT using specimens.

In conclusion, we assessed image quality in terms of demonstrating microcalcifications in DBT and FFDM. With our small study results, we suggest that image quality appears to be comparable with or better than conventional FFDM in terms of demonstrating microcalcifications, and visibility of microcalcifications on DBT is superior with 1 mm slab thickness compared with 5 or 10 mm thickness.

## Author Contributions

JB and JEL conceived and designed the experiments; analyzed the data; and contributed to the writing of the manuscript. JB wrote the first draft of the manuscript. JEL, ESC, JC, and JHK agree with manuscript results and conclusions. JB, JEL, ESC, JC, and JHK jointly developed the structure and arguments for the paper. JEL made critical revisions and approved final version. All authors reviewed and approved the final manuscript.

## Disclosures and Ethics

As a requirement of publication, author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality, and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. Any disclosures are made in this section.

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